UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/812,298	03/29/2004	Matthieu Guitton	AUR-2001US01	1803

41244 7590 04/01/2009

KEVIN M. FARRELL, PIERCE ATWOOD
ONE NEW HAMPSHIRE AVENUE, SUTIE 350
PORTSMOUTH, NH 03801

EXAMINER	
KIM, JENNIFER M	
ART UNIT	PAPER NUMBER
1617	
MAIL DATE	DELIVERY MODE
04/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/812,298	GUITTON ET AL.	
	Examiner	Art Unit	
	JENNIFER M. KIM	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/28/2008*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on December 29, 2008 has been entered.

Action Summary

The rejection of claims 1 and 4-9 under 35 U.S.C. 103(a) as being unpatentable over Tabuchi et al. (2002) in view of Donovan (U.S.Patent No. 6,265,379 B1) is being **maintained** for the reasons stated in the previous Office Action.

Response to Arguments

Applicants' arguments filed December 29, 2008 have been fully considered but they are not persuasive. Applicants argue that the present invention is not directed towards "protection against ischemic injury to the cochlea" but drawn to the treatment of tinnitus "induced by excitotoxicity and wherein treatment "suppresses or reduces NMDA receptor mediated aberrant activity of the auditory nerve". This is not found to be

persuasive because it is noted that the instant claims drawn to treatment of tinnitus induced by cochlear excitotoxicty that is provoked by ischemia. (see instant claims 1 and 4). Tabuchi et al. teach that ketamine showed protective effects on ischemia-reperfusion injury to the cochlea. (see page 48 right-hand column under conclusion). Tabuchi et al. also teach that ischemia induces acute swelling of the afferent dendrites on the basal side of the inner hair cells and the results strongly indicate that excitotoxicty is induced in the ischemic cochlea. (page 44 left-hand side, under introduction). Applicants assert on their response page 4 that excitotoxicty is defined in the art as the pathological process by which nerve cells are damages. Accordingly, the reference clearly teaches that ketamine is an effective agent for protection on ischemia-reperfusion injury of cochlea involving nerve cell damage was known at the time the invention was made. Therefore, the limitation of the suppression or reduction of NMDA receptor mediated aberrant activity of the auditory nerve is encompasses and obviated by the teaching.

Applicants argue that Tabuchi et al. describe the protection against hearing loss or protection against ischemic injury to the cochlea and not tinnitus, therefore, the pharmacological effect of the presently claimed invention was compared to the teachings of Tabuchi is distinct. This is not found to be persuasive because again, Tabuchi et al. teach that ketamine act as a protective agent for ischemic injury of cochlea wherein the injury involves excitotoxicity resulting in acute swelling of the afferent dendrites on the basal side of the inner hair cells. The treatment of tinnitus is cured by the Donovan reference who teaches that that tinnitus is cochlear nerve

dysfunction that is due to functional disturbances of the synapse between cochlear hair cells and afferent dendrites of the auditory nerve. Therefore, it would have been obvious to one of ordinary skill in the art to employ ketamine for the treatment of tinnitus induced by cochlear excitotoxicty provoked by ischemia because Tabuchi et al. teach the protective effect of ketamine in cochlear injury/dysfunction due to ischemic-reperfusion and because tinnitus is a disorder of cochlea due to functional disturbances involving auditory nerve as taught by Donovan. One would have been motivated to employ ketamine for the treatment of tinnitus in order to achieve an expected benefit of protection against cochlear damage due to ischemic-reperfusion resulting tinnitus well known condition due to cochlear dysfunction by Donovan.

Applicants argue that there is no scientific reason for the skilled person to test or employ ketamine for the treatment of tinnitus in view of the Tabuchi publication because Tabuchi's speculation that the effect of ketamine may be due to inhibition of nitric oxide release or enhancement of dopamine release. Tabuchi concludes from his findings, that agent MK-801 (another NMDA receptor antagonist) has no protective effect for hearing loss. Therefore, he suggests that any effect observed for ketamine is triggered via other pathways than NMDA receptor inhibition. This is not found to be persuasive because Tabuchi reference is clear that ketamine has protective effects against ischemia-reperfusion injuries involving excitotoxicity of cochlea. Therefore, it would have been obvious to employ ketamine for the treatment of tinnitus which is cochlea nerve dysfunction in order to achieve a protection of cochlea ischemic injury involving auditory nerve such as tinnitus.

Applicants argue that there was no model available at all in the art at the time of filing of the present application to determine the presence of tinnitus following excitotoxicity. This is not found to be persuasive because there is clear teaching that ketamine is useful for protection against ischemic injury of cochlea which causes tinnitus; there is a reasonable expectation of success in treating such disorder in vivo. It would have been obvious to one of ordinary skill in the art to employ ketamine for the treatment of tinnitus in human because it is next logical step next to Tabuchi et al's successful ketamine treatment against protection of cochlear injury due to ischemic-reperfusion.

Applicants argue that there is no indication in the disclosure of Donovan that the tinnitus model was anyhow related to cochlea ischemia or excitotoxicty in general. This is not found to be persuasive because Donovan teaches that tinnitus is a cochlear nerve dysfunction which is due to functional disturbances of the auditory nerve. Therefore, this teaching would motivate one of ordinary skill in the art to employ ketamine in human suffering from tinnitus in order to achieve an expected benefit of protection of cochlea in vivo experimentation demonstrated by Tabuchi et al. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1 and 4-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tabuchi et al. (2002) in view of Donovan (U.S.Patent No. 6,265,379 B1).

Tabuchi et al. teach that ketamine has protective effect against cochlear dysfunction induced by transient ischemia. (title). Tabuchi et al. teach that ketamine has protective effect against ischemia-reperfusion injury of the cochlea. (abstract). Tabuchi et al. teach that ketamine was administered intravenously. (page 45, left-hand column #1). Tabuchi et al. teach that ketamine showed protective effects on ischemia-reperfusion injury to the cochlea. (see page 48 right-hand column under conclusion). Tabuchi et al. also teach that ischemia induces acute swelling of the afferent dendrites on the basal side of the inner hair cells and the results strongly indicate that excitotoxicty is induced in the ischemic cochlea. (page 44 left-hand side, under introduction).

Tabuchi et al. do not expressly teach the treatment of tinnitus in human, site of local administration set forth in claims 5 and 6, and duration of cochlear excitotoxicty set forth in claims 7-9.

Donovan teaches that tinnitus, particularly inner ear tinnitus is due to cochlear nerve dysfunction that is due to functional disturbances of the synapse between cochlear hair cells and afferent dendrites of the auditory nerve. (column 2, lines 54-60).

Donovan teaches local administration for the treatment of tinnitus includes injection. (column 5, lines 62-67).

It would have been obvious to one of ordinary skill in the art to employ ketamine for the treatment of tinnitus induced by cochlear excitotoxicty provoked by ischemia because Tabuchi et al. teach the protective effect of ketamine in cochlear injury/dysfunction due to ischemic-reperfusion which induces excitotoxicity and because tinnitus is a disorder of cochlea involving auditory nerve as taught by Donovan. One would have been motivated to employ ketamine for the treatment of tinnitus in order to achieve an expected benefit of protection against cochlear damage due to ischemic-reperfusion resulting tinnitus well known condition due to cochlear dysfunction by Donovan. Further, it would have been obvious to one of ordinary skill in the art to employ ketamine for the treatment of tinnitus in human because it is next logical step next to Tabuchi et al's successful ketamine treatment against protection of cochlear injury due to ischemic-reperfusion. One would have been motivated to employ ketamine in human suffering from tinnitus in order to achieve an expected benefit of protection of cochlea in vivo experimentation demonstrated by Tabuchi et al. With regard to determining the duration of the disease states set forth in claims 7-9 is obvious because it is a part of routine medical examination/diagnosis to find out the severity of the disease state and to determine optimum medical care that is necessary. Further, the affected loci within the inner ear membrane to be administered is obvious because tinnitus occurs in inner ear, therefore, one of ordinary skill in the art would directly to, in or to the vicinity of the inner ear in order to optimize the protection of

cochlear damaged by ischemic-reperfusion. Moreover, the limitation of the suppression or reduction of NMDA receptor mediated aberrant activity of the auditory nerve is encompasses and obviated by the teaching of Tabuchi that ischemia induces excitotoxicty of cochlea.

Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

None of the claims are allowed.

Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER M. KIM whose telephone number is (571)272-0628. The examiner can normally be reached on Monday through Friday 6:30 am to 3 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Kim/
Primary Examiner, Art Unit 1617

Jmk
March 10, 2009